REMARKS

Claims 1-9, 11-19 and 22 are pending in this application. Claim 22 stands withdrawn. New claim 23 is added herein. Support for the new claim is provided by the specification at, e.g., page 10, line 7 through page 11, line 1, page 18, line 27 through page 19, line 4, and by the examples. No new matter is added. Entry of the new claim and reconsideration in view of the following remarks are respectfully requested. Following entry of the amendment, claims 1-9, 11-19, 22 and 23 are pending in this application.

Formal Matters

In the final Office Action mailed September 2, 2009, claim 22 was withdrawn by the Examiner, who stated that the Applicant was directed to elect a single photosensitizer for search and examination and that a search had already been made on the photosensitizer verteporfin, as detailed in the Office Action dated January 5, 2009.

Applicants respectfully call to the Examiner's attention that lemuteporfin was the species elected in response to a restriction requirement, as indicated in the Applicant's response filed October 17, 2008. In the Office Action dated January 5, 2009, the Examiner acknowledged the Applicant's election of lemuteporfin and extended the search to include verteporfin because the Examiner determined that the use of lemuteporfin for the treatment of hyperactive sebaceous gland disorders "does not appear to be taught or suggested by the prior art before the priority date of February 6, 2004." See Office Action dated January 5, 2009, at page 2.

Accordingly, Applicants respectfully request that the withdrawal of claim 22 as drawn to a non-elected species be withdrawn and that claim 22 be rejoined and examined on the merits.

Applicants note that new claim 23 is drawn to the use of lemuteporfin for the treatment of hyperactive sebaceous gland disorders, which the Examiner has acknowledged is not taught or suggested by the prior art.

The Rejections Under 35 U.S.C. § 103

Claims 1-9 and 11-19 remain rejected under 35 U.S.C. § 103(a) as allegedly unpatentable over Candela Corporation (WO 2003/086460) as evidenced by Olive Oil Chemistry (U) and in view of Bershad (U.S. Patent No. 6,096,765), for reasons of record. Applicants respectfully traverse the rejections for reasons of record, as well as at least the following reasons.

In rejecting the claims over Candela Corp., alone or in combination with Bershad and/or Olive Oil Chemistry, the Office relies upon the alleged overlap between the claimed fluence rate of between "about 0.1 mW/cm^2 and about 600 mW/cm^2" and the fluence rate range of "between about 100 W/cm^2 and about 40 MW/cm^2" disclosed in Candela Corp. at paragraph [0012]. The Examiner has taken the position that the fluence rate range in Candela Corp. is actually "between about 100 W/cm^2 and about 40 mW/cm^2."

The Applicants respectfully disagree, for at least the following reasons.

Prosecution history of the U.S. counterpart to Candela Corp. contradicts the Office's position

Applicants note that during the prosecution of the U.S. counterpart to Candela Corp., U.S. Application No. 10/407,921 (now abandoned), the applicants apparently recognized that the "40 MW/cm^2" value recited in their fluence rate range was in error. Candela Corp. amended claim 1, which recited a fluence rate range of between about 100 W/cm^2 and about 40 MW/cm^2 to recite a fluence rate of between about 100 W/cm^2 and about 40 kW/cm^2. See Response to Office Action in U.S. Application No. 10/407,921, filed December 19, 2005.

In their accompanying Remarks, Candela Corp. asserted that the amendment to the fluence rate in claim 1 was supported by paragraphs [0020] and [0050] of the original specification. (For the Examiner's convenience, a copy of the Office Action Response is attached as Exhibit A.)

Applicants note that the relevant portion of paragraph [0020] appears to be lines 29-31, disclosing that the peak fluence rate value of 4×10^4 Wcm^{-2} (i.e., 40 kW/cm^2) is the estimated threshold for a reduction in PDT efficacy due to saturation. Paragraph [0050] recites progressively

narrower fluence rate ranges from the range provided in paragraph [0012], down to 500 W/cm^2 to 1000 W/cm^2 (i.e., 0.5 to 1 kW/cm^2).

Applicants respectfully submit that this additional evidence contradicts the Examiner's conclusion that the "40 MW/cm^2" recited in paragraph [0012] of Candela Corp. was intended to be the lower end of the fluence rate range and is equivalent to "40 mW/cm^2." Rather, the amendments made in the counterpart U.S. case support the Applicant's contention that "40 MW/cm^2" is the upper limit of the disclosed range. In addition, the amendments suggest that the upper limit was likely intended to be 40 kW/cm^2, and that the recitation of "40 MW/cm^2" (i.e., megawatts/cm^2) was the result of an editorial error.

The Office has failed to rebut the Applicant's evidence of nonobviousness

The present Office Action fails to respond to the evidence presented in the Applicant's response filed on December 30, 2009. The Examiner has rejected the Rubinchik Declaration submitted under 37 CFR 1.132 with the response of December 30, 2009 as insufficient to overcome the rejection.

In particular, the Examiner states: "Applicant states that the fluence rate in the Candela reference is in megawatts, not milliwatts because of the capitalization of the letter M in MW/cm^2. In response, since the reference is drawn to application of Photodynamic therapy to skin it is extremely unlikely that Candela Corporation is applying megawatts to a patients [sic] skin since this is the equivalent of a lightening strike....[W]hen all of the evidence is considered, the totality of the rebuttal evidence of nonobviousness fails to outweigh the evidence of obviousness." See Office Action at pages 6-7.

Applicants note that the evidence presented is not limited merely to "the capitalization of the letter M in MW/cm^2." Rather, the Applicant's evidence relates to the entire context of the Candela Corp. reference, which the Examiner has improperly disregarded.

As noted previously, Candela Corporation describes the use of fluence rates that are considerably higher than those used in conventional PDT, at relatively low total light doses, which

are said to be advantageous to avoid side effects observed under conventional conditions, e.g., purpura. See WO 2003/086460 at, e.g., page 4, lines 16-19 and page 6, lines 10-13; see also the Rubinchik Declaration at ¶5.

If, as the Examiner contends, Candela Corp.'s fluence rate range is "between about 40 mW/cm^2 and about 100 W/cm^2", the range overlaps with the fluence rates for conventional light sources which Candela Corp. teaches cause side effects. See, e.g., Candela Corp. at paragraph [0003], stating: "These cw lasers and non-laser light sources are used at fluence rates of 10 to 500 milliwatts per square centimeter ($mWcm^{-2}$)" (emphasis added). Applicants note parenthetically that, according to convention, Candela Corp. recites the low end of this range (i.e., 10 $mWcm^{-2}$) first, and the high end of the range (i.e., 500 $mWcm^{-2}$) second.

No rationale has been provided to explain why Candela Corp.'s "high fluence rate" range would overlap with the fluence rate range they disclose for conventional light sources, which the reference discloses cause side effects that are overcome by their methods.

Second, Candela Corp. consistently uses two different abbreviations in two different contexts: "$mWcm^{-2}$", which is explicitly defined as "milliwatts per square centimeter" when describing fluence rates associated with conventional light sources (see Candela Corp. at paragraphs [0002]-[0005]), and "MW/cm^2" when describing the high fluence rates used in their methods (see Candela Corp. at paragraphs [0012] and [0050]).

As evidenced by the Rubinchik Declaration, one of ordinary skill in the art would reasonably interpret the consistent usage of two different terms in specific contexts as intended to convey different meanings. See the Rubinchik Declaration at ¶9. No basis has been provided to refute the Applicant's evidence or to explain why the drafters of Candela Corp. consistently used two different terms to mean the same thing.

Moreover, the conclusion that the "40 MW/cm^2" recited by Candela Corp. at paragraph [0012] actually means "40 mW/cm^2" requires concluding that the drafters recited the high end of the fluence rate range first. Applicants note this is contrary to convention and to the way Candela Corp.

rec tes every other range in the specification. For example, see: page 1, line 17: "500 to 650 nm"; page 1, line 26: "10 to 500 milliwatts per square centimeter"; page 2, line 4: "105-168 $mWcm^{-2}$"; page 2, lines 7-8: "between 550 and 700 nm and fluence rate 150 to 200 $mWcm^{-2}$"; page 2, line 12: "20 to 86 $mWcm^{-2}$", etc.

Again, no rationale has been provided to support the conclusion that the drafters inexplicably recited the high end of the fluence rate range first, and did so only in the case of their own fluence rate ranges.

The Examiner rejects as unpersuasive the Applicants argument that the exemplary conditions described at page 6, lines 27-31, or page 15, lines 18-20 and lines 23-24, would not be encompassed within the fluence rate range proposed by the Examiner. See, e.g., the Rubinchik Declaration at ¶¶10-11.

Applicants note that while exemplary conditions may not be limiting, it is clearly co interintuitive that the drafters of Candela Corp. would use conditions falling outside the scope of their invention when describing exemplary conditions. One of ordinary skill would reasonably expect the disclosed fluence rate range to encompass the proposed exemplary conditions.

The Examiner has failed to provide a rationale to explain any of these inconsistencies beyond a conclusory and unsubstantiated assertion that Candela Corporation *could not* have meant megawatts per square centimeter because the Examiner states that "this is the equivalent of a lightening strike."

Applicants note that the question is not whether Candela Corporation actually applied th: high end of their recited range to human skin, or whether they intended to use kW/cm^2 instead of MW/cm^2, but whether the disclosed range overlaps with the claimed range at all. It does not. Moreover, the Examiner's position ignores the extremely short irradiation times that are used in combination with Candela Corp.'s high fluence rates, to maintain relatively low overall fluences, in addition to localized nature of the treatment using such PDT methods.

As previously noted by the Applicants, the low end of Candela Corporation's range, 100 W/cm^2, is two orders of magnitude higher than the high end of the range recited in the instant claims, i.e., 600mW/cm^2. See, e.g., the Rubinchik Declaration at ¶12. Accordingly, *In re Wertheim* is inapplicable. In the absence of any overlap between the claimed fluence rate range and the range disclosed in Candela Corp., the Examiner has provided neither a motivation to practice the invention as claimed nor any reasonable expectation of successfully using substantially lower fluence rates than described in Candela Corp. while maintaining efficacy and providing an acceptable side effect profile.

As the Examiner has provided nothing substantive to contradict the evidence presented in the prior response and the Rubinchik Declaration, the Applicants submit that a *prima facie* case of obviousness has not been established. With regard to the secondary references, nothing in Bershad, alone or in combination with Candela Corp. as evidenced by Olive Oil Chemistry addresses the fundamental deficiencies in the Office's *prima facie* case over Candela Corp. alone.

In view of the foregoing remarks, Applicants submit that the invention is non-obvious over the cited art and respectfully request that the rejections under 35 U.S.C. § 103(a) be withdrawn.

Application No.: 10/588,419 Docket No.: 249692001700

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

In the event the U.S. Patent and Trademark office determines that an extension and/or other relief is required, applicant petitions for any required relief including extensions of time and authorizes the Commissioner to charge the cost of such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 249692001700. However, the Commissioner is not authorized to charge the cost of the issue fee to the Deposit Account.

Respectfully submitted,

Dated: August 19, 2010

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sd-511412

Application No.: 10/588,419 Docket No.: 249692001700

CONCLUSION

In view of the above, each of the presently pending claims in this application is believed to be in immediate condition for allowance. Accordingly, the Examiner is respectfully requested to withdraw the outstanding rejection of the claims and to pass this application to issue. If it is determined that a telephone conference would expedite the prosecution of this application, the Examiner is invited to telephone the undersigned at the number given below.

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Respectfully submitted,

Dated: August 19, 2010

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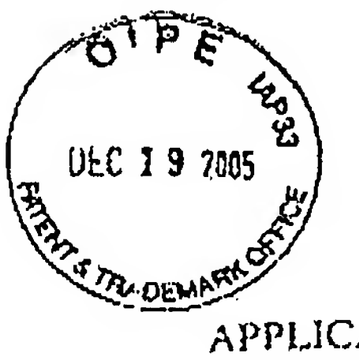

PATENT
Attorney Docket No.: CDL-034

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANTS:	Geronemus et al.	CONF. NO.	2742
SERIAL NO.:	10/407,921	GROUP NO.:	3739
FILING DATE:	April 4, 2003	EXAMINER:	Shay, David M.
TITLE:	High Fluence Rate Activation of Photosensitizers for Dermatological Application		

Mail Stop Amendment
Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

AMENDMENT AND RESPONSE

Dear Sir:

In response to the Office Action mailed from the U.S. Patent Office on June 20, 2005, in connection with the above-identified patent application, Applicants respectfully submit the following Amendment and Response. Applicants enclose herewith an Information Disclosure Statement (IDS) for your consideration, and hereby authorize the Commissioner to charge to Attorney's Deposit Account No. 50-3081 the requisite fees for the IDS, as well as an extension of time. In the event any additional fees are due, the Commissioner is hereby authorized to charge for this submission any such fees to Attorney's Deposit Account No. 50-3081.

Applicants respectfully request entry of this Amendment and Response.

- **Amendments to the Claims** begin on page 2 of this paper.
- **Remarks** begin on page 6.

Exhibit A
10/588,419

AMENDMENTS TO THE CLAIMS

1. (Currently amended) A method for treating a neoplastic or non-neoplastic dermatologic condition without causing purpura, the method comprising:

administering a photosensitizer or a pro-photosensitizer to a section of {[the]} skin affected with a neoplastic or non-neoplastic condition;

allowing the photosensitizer or pro-photosensitizer to accumulate in the section of skin {[tissue]} affected with the neoplastic or non-neoplastic condition; and

activating the photosensitizer or an endogenous photosensitizer formed from the pro-photosensitizer ~~irradiating the section of the skin~~ with a beam of light having a wavelength between about 500 nm and about 650 nm, a fluence rate of between about 100 W/cm^2 and about 40 kW/cm^2 ~~MW/cm^2~~, and a fluence of less than about 60 J/cm^2 to cause, ~~thereby causing~~ a therapeutic injury to the section of skin affected by the neoplastic or non-neoplastic condition without causing purpura of the skin.

2. (Original) The method of claim 1 wherein what is administered is a photosensitizer.

3. (Original) The method of claim 1 wherein what is administered is a pro-photosensitizer and wherein the pro-photosensitizer is allowed to metabolize in the skin tissue affected with the neoplastic or non-neoplastic condition.

4. (Original) The method of claim 2 wherein the photosensitizer comprises at least one of a chlorin, a cyanine, a purpurin, and a porphyrin.

5. (Original) The method of claim 4 wherein the porphyrin is benzoporphyrin derivative monoacid.

6. (Original) The method of claim 2 where the photosensitizer comprises at least one of a bacteriochlorin, a bacteriocyanine, a bacteriopurpurin, and a bacterioporphyrin.

7. (Original) The method of claim 2 wherein the photosensitizer comprises at least one of a

xanthenes and hypericin.

8. (Original) The method of claim 1 wherein the pro-photosensitizer comprises ALA.

9. (Original) The method of claim 8 wherein the pro-photosensitizer comprises an ALA derivative.

10. (Original) The method of claim 8 wherein the ALA derivative is an ALA ester.

11. (Original) The method of claim 8 wherein the ALA ester is ALA-methyl ester, ALA-n-pentyl ester, ALA-n-octyl ester, R,S-ALA-2-(hydroxymethyl)tetrahydr- opyranyl ester, N-acetyl-ALA, or N-acetyl-ALA-ethyl ester.

12. (Original) The method of claim 1 wherein the wavelength is between about 560 nm to about 600 nm.

13. (Original) The method of claim 1 wherein the wavelength is between about 600 nm and 650 nm.

14. (Original) The method of claim 1 wherein the beam of light is coherent.

15. (Original) The method of claim 1 wherein the beam of light is incoherent.

16. (Original) The method of claim 1 wherein the beam of light is continuous wave.

17. (Original) The method of claim 1 wherein the beam of light is pulsed.

18. (Original) The method of claim 1 wherein the fluence is less than about 30 J/cm^2.

19. (Original) The method of claim 1 wherein the fluence is less than about 20 J/cm^2.

20. (Original) The method of claim 1 wherein the fluence is less than about 12.0 J/cm^2.

21. (Original) The method of claim 1 wherein the fluence is less than about 7.5 J/cm^2.

22. (Original) The method of claim 17 wherein the a pulse duration is between about 1 microsecond and about 200 milliseconds.

23. (Original) The method of claim 22 wherein the pulse duration is between about 10 microsecond and about 10 milliseconds.

24. (Currently amended) The method of claim 1 wherein the beam of light has a fluence rate of between about 500 W/cm^2 and about 20 kW/cm^2 ~~MW/cm^2~~.

25. (Original) The method of claim 1 wherein allowing the photosensitizer or pro-photosensitizer to accumulate and metabolite in the skin tissue comprises waiting for between about 0.1 to about 48 hours post-administration of the photosensitizer or pro-photosensitizer before irradiation.

26. (Original) The method of claim 1 wherein the neoplastic dermatological condition comprises at least one of actinic keratosis, skin cancer, Bowen's disease, and dysplasia,

27. (Original) The method of claim 1 wherein the non-neoplastic dermatological condition comprises at least one of verrucae vulgaris, acne vulgaris, acne conglobata, acne comedonica, papularpustular acne, acne inversa, acne fulminans, back acne, acne mechanical rosacea, sebaceous hyperplasia, oily skin, lichen planus, psoriasis, and eczema.

28. (Original) The method of claim 1 where the non-neoplastic dermatologic condition comprises at least one of unwanted hair, photoaged skin, and wrinkles.

29. (Original) The method of claim 1 wherein the photosensitizer or pro-photosensitizer is administered orally, topically, or parenterally.

30. (Original) The method of claim 1 wherein the photosensitizer or pro-photosensitizer is administered as a component of a formulation comprising a pharmaceutically acceptable carrier or excipient.

31. (Original) The method of claim 1 wherein the therapeutic injury results in the reduction of at least one of the surface area, the depth, and the amount of the skin affected by the neoplastic or non-neoplastic condition.

32. (Original) The method of claim 1 further comprising heating the section of the skin with a pulse of radio frequency before, during, or after the irradiation of the section of the skin with a beam of light.

33. (Currently amended) A method for treating a neoplastic or non-neoplastic dermatologic condition without causing purpura, the method comprising:

applying a pro-photosensitizer to a section of [[the]] skin affected with a neoplastic or non-neoplastic condition;

allowing the pro-photosensitizer to accumulate and metabolize in the section of skin [[tissue]] affected with the neoplastic or non-neoplastic condition; and

activating an endogenous photosensitizer formed from the pro-photosensitizer ~~irradiating the section of the skin~~ with a pulsed laser beam having a wavelength between about 500 nm and 650 nm, a fluence less than about 20 J/cm^2, and a pulse duration between about 10 microseconds and 40 milliseconds to cause, ~~thereby causing~~ a therapeutic injury to the section of skin affected by the neoplastic or non-neoplastic condition without causing purpura of the skin.

34. (New) A method for treating a neoplastic or non-neoplastic dermatologic condition without causing purpura, the method comprising:

administering a photosensitizer or a pro-photosensitizer to a target area of skin affected with a neoplastic or non-neoplastic condition;

allowing the photosensitizer or pro-photosensitizer to accumulate in the target area of skin affected with the neoplastic or non-neoplastic condition; and

activating the photosensitizer or an endogenous photosensitizer formed from the pro-photosensitizer with a pulsed laser beam having a wavelength between about 585 nm and about 600 nm, a fluence of less than about 20 J/cm^2, and a pulse duration between about 10 microseconds and about 40 milliseconds to cause a therapeutic injury to the target area affected with the neoplastic or non-neoplastic condition without causing purpura of the skin.

REMARKS

Claims 1-33 are currently pending. Claims 1, 24, and 33 are herein amended. New claim 34 is herein added. After entry of this amendment, claims 1-34 will be pending. Support for the amendments to claims 1 and 33 can be found in the claims as originally filed and at least in paragraphs [0017] and [0024] of the specification as originally filed. Support for new claim 34 can be found in the claims as originally filed and at least in paragraphs [0049] to [0053] of the specification as originally filed. Support for the amendment to the fluence rate in claims 1 and 24 can be found in the claims as originally filed and at least in paragraphs [0020] and [0050] of the specification as originally filed. Applicants believe that no new matter is introduced by these amendments.

Applicants enclose herewith an Information Disclosure Statement for consideration by the Examiner. Two of the references cited, C21 and C24, are being resubmitted because it appears the Examiner did not receive complete copies. The other three references, C63-65, are being submitted for the first time.

Rejections Under 35 U.S.C. §103(a)

Claims 1-33 are rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over a publication by Kalka et al. ("Kalka") in combination with U.S. Patent No. 6,902,563 to Wilkens et al. ("Wilkens"). In particular, the Office action asserts on page 2 that Kalka discloses the use of various photosensitizers to photodynamically treat neoplastic and non-neoplastic conditions and Wilkens teaches the use of pulsed irradiance and fluence values to treat various dermatological conditions. Further, the Office action suggests that it would have been obvious to employ the pulse parameters of Wilkens in the method of Kalka since Kalka frequently does not teach the proper parameters and since "the use of pulsed radiation generates higher levels of singlet oxygen, reaches deeper layers of skin, and operates more efficiently than CW radiation." Alternatively, the Office action suggests that it would have been obvious to employ the photosensitizers of Kalka in the method of Wilkens since Wilkens does not discuss photosensitizers and "the use of photosensitizers is known to provide superior treatment to irradiation alone, official notice of which is [] taken" by the Examiner. Applicants respectfully traverse this rejection to the extent that it is maintained over the claims as amended.

I. Kalka and Wilkens fail to teach each and every element of the independent claims.

Applicants respectfully submit that claims 1-34 are patentable over Kalka and Wilkens, individually or in combination. Independent claims 1, 33, and 34 are directed to methods for treating a dermatologic condition without causing purpura of the skin. The methods include using a beam of radiation or a pulsed laser beam having a wavelength between 500 nm and 650 nm (or between 585 nm and 600 nm) and a high fluence rate to activate a photosensitizer.

As Applicants disclose in their specification, "[t]he method of the invention is based on the surprising discovery that a high fluence rate can be used for effective treatment while the overall fluence is kept below the purpura threshold." [Paragraph [0011] of Applicants' specification as filed.] Furthermore, based on the understanding of the mechanisms of photodynamic therapy at the time of the invention, "the low light dosage and the very high fluence rate used in the present invention would both be expected to limit the efficacy of treatment. However, according to the present invention the use of a laser at relatively low light dosage and high fluence rate is not only effective but advantageous." [Paragraph [0021] of Applicants' specification as filed.]

While Kalka discloses using photosensitizers and pro-photosensitizer to treat various conditions, Kalka fails to teach or suggest using a beam of radiation with a wavelength between 500 nm and 650 nm and the parameters claimed to treat a condition without causing purpura of the skin. Kalka states "[w]avelengths shorter than 600 nm are absorbed mainly by hemoglobin, whereas water absorbs wavelengths longer than 1200 nm, restricting the 'therapeutic window' of the skin to 600 to 1200 nm." [Last sentence of second full paragraph of page 394 of Kalka.] In contrast, Applicants purposefully operate in a wavelength region where hemoglobin and deoxyhemoglobin strongly absorb, e.g., between 500 nm and 650 nm (See Figure 2 of Applicants' specification), because they have discovered irradiation parameters (pulse duration and light dose) that can effectuate a treatment that does not result in purpura caused by excessive the heating of a blood vessel or components of blood. [Paragraph [0042] of Applicants' specification.] Furthermore, Wilkens not only does not discuss photosensitizers in relation to his treatment, Wilkens also fails to teach or suggest a treatment that does not cause purpura of the skin.

Accordingly, the combination of Kalka and Wilkens fails to teach each and every element of independent claims 1, 33, and 34, either explicitly or impliedly, and, therefore, fails to support a *prima facie* case of obviousness. Applicants respectfully request that the rejection under 35 U.S.C. §103 be reconsidered and withdrawn. Furthermore, Applicants respectfully submit that claims 2-32 are allowable as depending from base claim 1.

II. Employing the pulse parameters of Wilkens in the method of Kalka is not obvious.

The Office action suggests that it would have been obvious to employ the pulse parameters of Wilkens in the method of Kalka since Kalka frequently does not teach the proper parameters and since Wilkens reports that "the use of pulsed radiation generates higher levels of singlet oxygen, reaches deeper layers of skin, and operates more efficiently than CW radiation." Kalka contradicts this assertion stating instead "[t]he comparison of continuous-wave and pulsed lasers in clinical PDT has shown no difference in the cure rate." [First full sentence of page 395 of Kalka.] Therefore, Kalka does not suggest that pulsed radiation is more efficient than CW radiation, and Kalka does not motivate one skilled in the art to employ Wilkens pulsed beam parameters in the method of Kalka. Indeed, Kalka and Wilkens teach away from such a combination.

Furthermore, Wilkens's parameters are optimized for a treatment that does not use photosensitizers. Wilkens states that "[s]ystemic or topical dyes are not administered, so that the described procedure is not a [photodynamic therapy] PDT." [Column 12, lines 63-64.] Accordingly, there is no teaching or suggestion in Kalka that using the non-PDT parameters of Wilkens in a PDT technique of Kalka would result in an effective treatment without causing purpura. Moreover, there is no teaching or suggestion in Wilkens that Wilkens's non-PDT parameters can be used in any PDT technique to effectuate a treatment that does not cause purpura.

Accordingly, because one skilled in the art would not be motivated to employ the pulse parameters of Wilkens in the method of Kalka, Applicants respectfully submit that the combination of Kalka and Wilkens fails to support a *prima facie* case of obviousness against independent claims 1, 33, and 34. Applicants respectfully request that the rejection under 35

U.S.C. §103 be reconsidered and withdrawn. Furthermore, Applicants respectfully submit that claims 2-32 are allowable as depending from base claim 1.

III. Employing the photosensitizers of Kalka in the method of Wilkens is not obvious.

Even if the Examiner maintains that employing the photosensitizers of Kalka in the method of Wilkens does teach each and every element of any independent claim, Applicants respectfully submit that the cited references do not provide adequate motivation or suggestion to combine their teachings. Indeed, they teach away from such a combination. Wilkens relies on direct absorption of endogenous chromophores, and explicitly rejects the use of photosensitizers. Wilkens states that "[s]ystemic or topical dyes are not administered, so that the described procedure is not a [photodynamic therapy] PDT." [Column 12, lines 63-64.] To introduce a photosensitizer to the method of treatment of Wilkens would change the principle of operation of Wilkens's invention, i.e., a photosensitizer would be activated upon irradiation instead of direct activation of an endogenous chromophore as disclosed by Wilkens, and Wilkens's invention would be rendered unsatisfactory for its intended purpose, i.e., to provide an irradiation device for therapeutic purposes that does not rely on a photosensitizer.

Furthermore, to make this rejection, the Examiner relies on official notice. According to MPEP 2144.03, official notice unsupported by documentary evidence should only be taken by the examiner where the facts outside the record are "capable of instant and unquestionable demonstration as being well-known" in the art. Applicants respectfully submit that the fact officially noticed by the Examiner, i.e., the use of photosensitizers is known to provide superior treatment to irradiation alone, is not well-known in the art and is not capable of demonstration.

While the combination of light and photosensitizers to treat certain skin disorders is known, some neoplastic or non-neoplastic condition and disorders can be treated satisfactorily without a photosenitizer. Wilkens, for example, discloses a method and device for therapeutic treatment without using photosensitizer, and this directly undermines Examiner's position. Furthermore, photothermolysis is widely used by practitioners to treat cosmetic and dermatologic disorders. Accordingly, Applicants do not believe that the use of photosensitizers is known to provide superior treatment to irradiation alone. In the event the Examiner chooses to maintain this assertion, Applicants respectfully request that the Examiner provide prior art or an affidavit

or declaration setting forth specific factual statements and explanation to support his finding. [MPEP 2144.03 and 37 CFR 1.104(d)(2).]

Regardless, Applicants respectfully submit that the claimed invention is nonetheless patentable even if the Examiner maintains his assertion of official notice. Both Kalka and Wilkens have been discussed above and Applicants reiterate here that (i) Kalka does not teach, suggest, or motivate using the non-PDT parameters of Wilkens in a PDT technique of Kalka would result in an effective treatment without causing purpura, (ii) Wilkens does not teach, suggest, or motivate that Wilkens's non-PDT parameters can be used in any PDT technique to effectuate a treatment that does not cause purpura, and (iii) incorporating a photosensitizer into the method of Wilkens would destroy its principle of operation.

Accordingly, because one skilled in the art would not be motivated to employ the photosensitizers of Kalka in the method of Wilkens, Applicants respectfully submit that the combination of Kalka and Wilkens fails to support a *prima facie* case of obviousness against independent claims 1, 33, and 34. Applicants respectfully request that the rejection under 35 U.S.C. §103 be reconsidered and withdrawn. Furthermore, Applicants respectfully submit that claims 2-32 are allowable as depending from base claim 1.

Non-Statutory Double Patenting Rejection

Finally, the Office action rejects the pending claims under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-34 of copending Application No. 10/241,273 ("'273"). The Office action asserts that although the claims are not identical, they are not patentably distinct because the claims of the '273 patent application "anticipate" the instant application claims. Applicants respectfully transverse this basis of rejection, to the extent is maintained over the claims as amended.

For the reasons stated above, Applicants believe that claims 1-34 of the instant application are in condition for allowance. Because the double patenting rejection is provisional, Applicants respectfully request that the examiner withdraw the double patenting rejection and allow the application to issue as a patent.

Furthermore, Applicants respectfully suggest that regardless of the status of the other,

non-double patenting rejections, the double patenting rejection is improper because the instant claims are not obvious in view of the claims of the '273 application. Applicants respectfully submit that the claims of the '273 application fails to teach, suggest, or motivate each and every element of claims 1-34 of the instant application either explicitly or implicitly. For example, claims 1-34 of the instant application require activating a photosensitizer to treat a condition without purpura of the skin. In contrast, '273 explicitly teaches causing purpura. '273 claims a method combining selective photothermolysis of blood vessels and activation of a photosensitizer to ameliorate a lesion or disorder. "The parameters of the pulsed or scanned beam of electromagnetic radiation should be sufficient to induce photothermolysis of blood vessels and create purpura in the target region." [Specification of '273 application at page 7, line 7.]

Accordingly, because a provisional double patenting rejection is the only basis of rejection remaining and because the instant claims are patentably distinct from the claims of the '273 application, Applicants respectfully request that the provisional double patenting rejection be reconsidered and withdrawn and that claims 1-34 of the instant application be allowed to issue.

CONCLUSION

In view of the foregoing, Applicants respectfully submit that the claims are in condition for allowance and request early favorable action. If the Examiner believes a telephonic interview would expedite the prosecution of the present application, the Examiner is welcome to contact Applicants' agent at the number below.

Respectfully submitted,

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